CASE REPORTS

Metastasizing Adenocarcinomas of the Tarsal Glands

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ADENOCARCINOMAS arising from the skin appendages of the eyelids are rare. Most of the tumors at that site reported in the literature are sebaceous gland carcinomas arising from meibomian glands and very few are carcinomas of sweat glands or the glands of Moll. Sweat gland carcinomas are much more common than sebaceous gland carcinomas in other areas in the skin, but most sebaceous gland carcinomas occur in the eyelid. Due to a considerable variance in the reported criteria and terminology, and because many of the tumors are very well differentiated, it is difficult to determine the exact number of cases of tarsal gland carcinomas in the literature. In this review, we included all adenocarcinomas that were primary in the eyelid and that had metastasized and therefore could be accepted as being malignant. This review was undertaken when we observed a case, the clinical features of which conform to those described for some sebaceous gland carcinomas, but the pathologic pattern of which was unusual, suggesting an origin in the glands of Moll.

Report of a Case

A 64-year-old Caucasian man entered the hospital on January 26, 1964, because of a mass in the right lower eyelid of four years' duration. He had consulted an ophthalmologist, not long before, because of "rapid growth." A biopsy specimen appeared benign on pathologic examination, but because of the increasing size of the lesion complete excision was recommended.

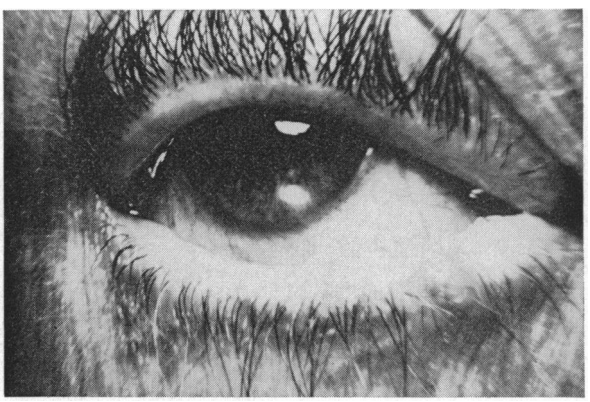

Figure 1.—Appearance of tumor before excision (Courtesy, Dr. S. Castanares).

On examination of the eyes a site of peripheral iridectomy was noted on the left eye. There was a 3 mm tumor on the right lower eyelid involving the palpebral margin, the skin adjacent to the palpebral margin and the conjunctiva. On January 27, 1964, under block anesthesia, a complete through-and-through wedge excision of the tumor-containing portion of the right lower lid was performed. The excision included the skin, orbicularis, tarsus and conjunctiva. A lateral canthoplastic lid reconstruction then was carried out.

Pathologist's report: The resected specimen was a wedge-shaped portion of the eyelid measuring 0.7 cm in greatest dimension. On the lid margin there was a 0.3 cm, flat, smooth, gray lesion extending into the underlying stroma. Microscopically, the small tumor was found to be lobulated, to extend close to the overlying epidermis, but to penetrate fairly deeply into the underlying stroma, partially surrounding hair follicles and meibomian

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glands. The tumor was papillary and microcystic, the individual delicate papillary processes being covered by single and occasionally multiple layers of cuboidal epithelial cells with very uniform, round and oval nuclei and a prominently vacuolated cytoplasm, the individual vacuoles being small and confluent. The tumor was locally completely excised, and was considered to be a papillary adenoma of sweat gland origin.

The patient was next admitted on August 24, 1964, because of a mass in the right pre-auricular area which he had noted three years previously, but which had become progressively larger over the past six months. This pre-auricular mass was not described on his admission in January 1964, but was noted by one examiner as a "right, pre-auricular, firm, freely movable mass" on his admission in October 1963, for a cataract extraction of the left eye. The physical examination showed a 2 × 4 cm soft, freely movable, right pre-auricular mass and was otherwise unremarkable. The preoperative diagnosis was probable right parotid tumor. On August 25, 1964, under general anesthesia, a 2 × 4 cm, gray, cystic mass was excised. It appeared to be adjacent to the parotid gland and was removed easily with blunt dissection. The patient was discharged on August 29, 1964.

The excised specimen consisted of two multilocular, lobulated, intact cystic structures measuring 3.8 × 3.0 and 2.6 × 2.0 cm. Sections showed the individual cystic compartments to measure up to 2 cm in diameter and to contain yellowish, cloudy, slightly mucoid fluid. The walls of the individual cystic compartments were thin and semitranslucent. A frozen section showed an epithelial, in areas papillary, cyst lining. The subsequent microscopic examination showed the individual cystic compartments to be lined by single and multiple layers of epithelial cells, most of which contained round or oval hyperchromatic nuclei and prominent clear vacuoles in the cytoplasm. In portions of the wall, there were solid nests and groups of glands formed by similar or occasionally more anaplastic epithelial cells with large nuclei and more prominent nucleoli. Papillary structures formed by these cells extended into individual cystic compartments. The compartments were surrounded by fibrous connective tissue septa which were slightly infiltrated by lymphocytes. The tumor was located within parotid tissue of which a rim was seen in the periphery. However,

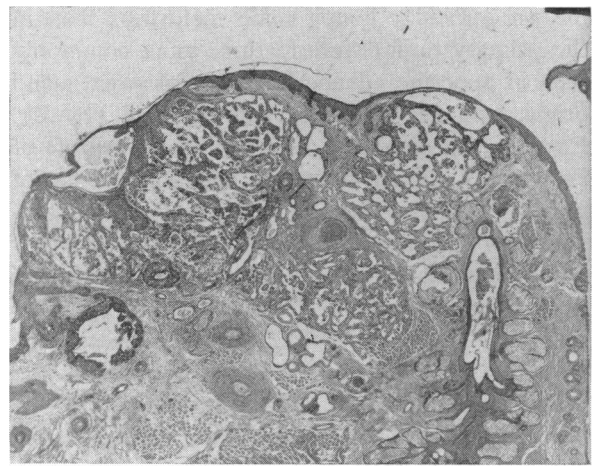

Figure 2.—Photomicrograph (× 30) showing the entire excised tumor from the eyelid. Note the papillary features and close proximity to many of the specialized skin appendages.

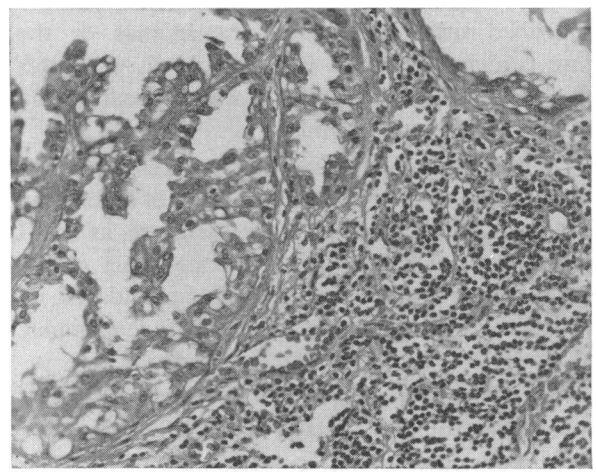

Figure 3.—Photomicrograph (× 250) of the metastatic lesion in pre-auricular lymph nodes. The typical histologic pattern with a prominently foamy cytoplasm of many of the cells is demonstrated.

several of the nests of cystic and glandular structures were found within lymphoid tissue, indicating that the tumor was metastatic to a lymph node rather than a salivary gland tumor. The histologic pattern was very similar to that previously seen in the tumor of the right lower eyelid.

Discussion

The pathologic features in the present case were unusual; they did not resemble those previously described in skin appendage carcinomas of the eyelid. The foamy cytoplasm and the overall cytologic appearance resembled those of sebaceous gland carcinoma. However, the papillary configuration and the cyst formation, more prominent in

the pre-auricular lymph node metastasis than in the primary tumor were features more commonly seen in apocrine adenocarcinomas of sweat gland origin, and the tumor was interpreted (by Dr. Elson B. Helwig of the Armed Forces Institute of Pathology) as an apocrine adenocarcinoma of glands of Moll. There was, however, no resemblance of the pattern to that described in the very few references of carcinoma supposedly arising from the glands of Moll. Whorton and Patterson[23] described a case in which they demonstrated a transition from glands of Moll to tumor, but the described tumor itself was characterized by the occurrence of the tumor cells in the forms of cords and a solid pattern, quite contrary to the cystic and somewhat papillary pattern seen in the present case. Since origin of the tumor from glands of Moll was not unequivocally demonstrated, and as the histologic features conformed neither to the described meibomian gland carcinomas or the rare carcinomas of the glands of Moll, we prefer to classify the lesion simply as an adenocarcinoma of specialized tarsal glands.

Clinically, the case did have features similar to those reported in several of the cases of carcinoma of tarsal glands collected in the literature, as noted in Table 1. All cases of adenocarcinoma of the eyelid apparently arising in skin appendages, in which there was definite evidence of malignancy as shown by metastasis, are included.

Of the 15 previously reported cases with known metastasis from tarsal gland adenocarcinoma, nine were reported as arising in meibomian glands. Five cases were reported as either sebaceous or tarsal gland carcinoma without note as to specific origin. The primary tumor site was in the upper lid in nine cases, in the lower lid in four; and in three cases the site was not stated. This predilection for the upper lid is consistent with the greater number of meibomian glands in the upper than in the lower lids.[19] Stout and Cooley[20] described a case involving the sweat glands of the eyelid with metastasis, but so far as we could determine there have been no reported cases of metastasis of tumors of the glands of Zeis or Moll. In a case reported by Whorton and Patterson[23] of an apparent carcinoma of Moll's glands, there was associated extramammary Paget's disease of the overlying skin as well as a palpable parotid lymph node, which subsequently, however, disappeared. There was no mention of metastasis in Scheie's[15] case of adenocarcinoma of the glands of Zeis. The latter two cases were, therefore, not included in our tabulation.

As was noted by Straatsma,[19] the pre-auricular or parotid lymph nodes are the most frequent sites of metastasis (nine of sixteen cases). Supraclavicular, cervical or submaxillary nodes may be involved. Distant metastasis also occurs, however.[8,10,20]

It is interesting that our patient noted the eyelid tumor four years before admission, and the pre-auricular nodes six months later, but the onset of progressive enlargement of the metastatic lesion did not occur until the primary tumor had been removed. An accelerated rate of growth after incomplete excision or curettage with early recurrences and metastasis has been described by other observers.[4,19,21] The primary tumor in our patient, however, had been completely excised following the initial biopsy.

To distinguish tarsal gland adenocarcinomas from a chalazion may be very difficult.[3,5,14] The importance of this distinction and the awareness that the combination of a pre-auricular, parotid or cervical mass and a small "chalazion" may represent tarsal gland carcinoma with metastasis, has been emphasized.[6,19,21]

The prognosis for tarsal gland carcinoma is unfavorable once metastasis has occurred. At the time of publication of the reports of the 16 cases reviewed, seven of the patients had died of metastatic disease. The cases as selected represent the least favorable group of tarsal gland carcinomas, since metastasis had already occurred, but most of the tumors were very well differentiated and some had a long course up until the time of biopsy or excision, as was the case in the patient herein reported upon. Subsequent to diagnosis and excision, rapid recurrence and local extension were often noted.[1,20,24] Orbital exenteration was required in at least three cases. All patients had been treated with surgical excision and some with subsequent radiotherapy. Only two patients were followed for an extended period, one of them surviving for 11 years,[10] and one being alive and well 15 years after excision of both the primary tumor and the lymph node metastastic lesion and subsequent radiotherapy.[12]

Summary

A case of tarsal gland adenocarcinoma in a 64-year-old male is described. The primary tumor in the right lower eyelid was quite small and was

TABLE 1.—*Clinical Data on 16 Cases of Adenocarcinomas of Tarsal Glands*

Author	*Year*	*Sex and Age*	*Duration of Symptoms*	*Type and Site of Primary Tumor*	*Site of Metastasis*	*Treatment*	*Follow-Up*	*Remarks*
Sourdille[17]	1894	M-59	.....	Sebaceous gland carcinoma, upper eyelid	Preauricular lymph nodes	Curettage	.....	Rapid growth-recurrence 12 days after curettage
Snell[16]	1908	F-63	10 years	Meibomian gland carcinoma, upper eyelid	.....	Excision exenteration	.....	Recurrence with metastasis even after exenteration
Cavara[2]	1920	M-67	Few months	Sebaceous gland carcinoma, upper eyelid	Preauricular lymph nodes	Exenteration with lymph node excision	Died of tumor	Recurrence 6 months postoperatively
Hagedoorn[6]	1934	M-66	2 years	Meibomian gland adenocarcinoma, upper eyelid	Preauricular and supraclavicular lymph nodes	Excision	Died of tumor	Nodes excised 4 years after removal of primary. Died 4 months postoperatively
Knapp[8]	1936	F-59	.....	Meibomian gland adenocarcinoma, upper eyelid	Preauricular and nodes on side of face and neck, abdominal tumor	Excision, radium	Died of tumor	.....
Pages et al.[13]	1938	M-33	3 weeks	Sebaceous gland carcinoma	.....	Excision, x-ray therapy	.....	Metastasis present at operation. Recurrence and metastasis disappeared with x-ray therapy
Magnus[10]	1947	M-79	11 years	Meibomian gland adenocarcinoma, lower eyelid	Liver	Excision	Died of tumor	Had "ulcerated tumor" removed right lower lid 11 years prior to death. No pathology report of specimen
Spaeth[18]	1951	.....	.....	Adenocarcinoma tarsus	Cervical and submaxillary glands	.....	.....	.....
Spaeth[18]	1951	.....	.....	Adenocarcinoma, tarsus	Lip with extension to nose and malar bone	.....	Died	.....
Ibrahim[7]	1951	M-73	1 year	Meibomian gland adenocarcinoma, upper tarsus	Preauricular node	Excision, postoperative irradiation	1 year	Node excised 6 months after removal of primary
Stout and Cooley[20]	1951	F-44	2 months	Sweat gland carcinoma, lower eyelid	Ethmoid bone, lung	Excision, x-ray therapy, exenteration	Died	Exenteration after 2 re-excisions and x-ray therapy. Died 2 years after onset and 22 months after first operation
Straatsma[19]	1956	.....	.....	Meibomian gland carcinoma, upper eyelid	Preauricular lymph node	Excision	15 years	Postoperative radiation therapy, primary lesion and node excised simultaneously
Sweebe and Cogan[21]	1959	F-64	6 months	Meibomian gland adenocarcinoma, lower eyelid	Orbit preauricular node	Excision radical neck dissection 6 months later	Died	Died of cardiac failure 36 hours after radical neck dissection
Sweebe and Cogan[21]	1959	M-79	.....	Meibomian gland adenocarcinoma, upper eyelid	Preauricular and cervical lymph nodes	Excision of mass and nodes	Died	Lost 30 pounds 7 months after excision. 7 months postoperatively had large mass palpable in right upper quadrant. No autopsy
Mangubat and Garcia[11]	1961	F-62	2 years	Meibomian gland carcinoma, upper eyelid	Regional lymph nodes	Excision postoperative radiation	.....	.....
Gowey and Kern	1965	M-64	4 years	Tarsal gland adenocarcinoma, lower eyelid	Preauricular lymph nodes	Excision		Rapid growth of preauricular lymph node after biopsy and subsequent excision of primary tumor

completely excised, but metastasis to right pre-auricular lymph nodes had occurred. In a review of the literature reports were found of 15 similar cases of tarsal gland carcinoma, most of which had originated in meibomian glands. Because of the high incidence of metastasis, a diagnosis of tarsal gland carcinoma should be considered in patients with often small tumors in the eyelid, particularly in the presence of palpable pre-auricular nodes.

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REFERENCES

1. Beach, A., and Severance, A. O.: Sebaceous gland carcinoma, Ann. Surg., 115:258, 1942.

2. Cavara, V.: Cited by Beach and Severance.[1]

3. Das, S. P.: Adenocarcinoma of meibomian glands, J. All-India Ophthal. Soc., 10:36, 1962.

4. Duke-Elder, S.: Textbook of Ophthalmology, Vol. 5, The C. V. Mosby Company, St. Louis, 1952, pp. 5065-5069.

5. Friedenwald, J. S., and Steward, H. K.: Ophthalmic Pathology: An Atlas and Textbook, W. B. Saunders Company, Philadelphia, 1952, p. 197.

6. Hagedoorn, A.: Adenocarcinoma of a meibomian gland, A.M.A. Archives Ophth., 12:850, 1934.

7. Ibrahim, A. H.: Adenocarcinoma of the meibomian gland, J. Roy. Egypt. M. A., 34:42, 1951.

8. Knapp, A. In discussion on O'Brien.[12]

9. Lever, W. F.: Histopathology of the Skin, Ed. 3, J. B. Lippincott Company, Philadelphia, 1961, p. 493.

10. Magnus, J. A.: Adenocarcinoma of meibomian gland with secondaries in the liver, Tr. Ophth. Soc. U. Kingdom, 67:426, 1947.

11. Mangubat, L. L., and Garcia, F. V.: Carcinoma of the meibomian glands, Philippine J. Surg. and Surg. Subspec., 16:321, 1961.

12. O'Brien, C. S., and Braley, A. E.: Common tumors of the eyelids, J.A.M.A., 107:933, 1936.

13. Pages, R; Stora, E., and Duguet, J.: Cited by Beach and Severance.[1]

14. Reese, A. B.: Tumors of the Eye, Paul B. Hoeber, Inc., New York, 1951, pp. 5-7.

15. Scheie, H. G., Yanoff, M., and Frayer, W. C.: Carcinoma of sebaceous glands of the eyelid, A.M.A. Arch. Ophth., 72:800, 1964.

16. Snell, S.: Carcinoma of the orbit originating in a meibomian gland, Tr. Ophth. Soc. U. Kingdom, 23:144, 1907-1908.

17. Sourdille, Cited by Beach and Severance.[1]

18. Spaeth, E. B.: Ocular tumors, A.M.A. Arch. Ophth., 46:421, 1951.

19. Straatsma, B. R.: Meibomian gland tumors, A.M.A. Arch. Ophth., 56: 71, 1956.

20. Stout, A. P., and Cooley, S. G.: Carcinoma of sweat glands, Cancer, 4:521, 1951.

21. Sweebe, E. C., and Cogan, D. G.: Adenocarcinoma of the meibomian gland, A.M.A. Arch. Ophth., 61:282, 1959.

22. Warren, S., and Warvi, W. N.: Tumors of sebaceous glands, Am. J. Path., 19:441, 1943.

23. Whorton, C. M., and Patterson, J. B.: Carcinoma of Moll's glands with extramammary Paget's disease of the eyelid, Cancer, 8:1009, 1955.

24. Wooton, H. W.: A Case of adenocarcinoma of the upper eyelid subsequently extending to the orbit, A.M.A. Arch. Ophth., 56:275, 1927.

Sporotrichosis in California

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SPEED AND EASE OF TRAVEL may result in the transplantation of endemic diseases into new areas. In some instances, the causative organism may be transported in products, baggage or vehicles. In others, prolonged incubation periods may result in the appearance of manifestations of the disease long after the patient has departed from the geographic area in which he was infected. For instance, Harrell and Honeycutt reported on 12 patients who acquired coccidioidomycosis in California or Arizona but in whom the infection was diagnosed in southeastern Michigan.[3]

Sporotrichosis is endemic in the midwest, especially in the Mississippi Valley. According to Phillips and Baritel,[4] seven patients with this disease had been reported from California up to January 1, 1947, out of 256 recorded cases of this mycosis. No further reports of sporotrichosis in California were uncovered after that date. In fact, the only other mention of this infection in this state was in an investigative article from Los Angeles discussing the distribution of I^{131} in lesions of sporotrichosis produced experimentally in mice.[5]

In most of the seven patients, it was impossible to trace the source of infection. Unknown to the physicians reporting the case, one patient had returned from a camping trip in the Mississippi Valley not long before the disease was diagnosed. The following patient is presented as an example of sporotrichosis of industrial origin in which the infection, diagnosis and cure occurred within the boundaries of California. Of course, the assumed source of the infection (a cat) may have reached California from a recognized endemic area. A similar case of sporotrichosis due to the bite of a cat that was being destroyed was reported by Conkwright.[2]

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